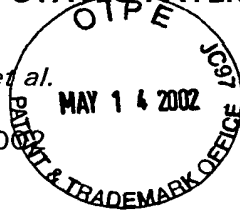


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: FREDEKING *et al.*
Serial No.: 10/038,557
Filed: January 3, 2002
Confirmation No.: 8399



For: *COMPOSITIONS AND METHODS
FOR TREATING HEMORRHAGIC
VIRUS INFECTIONS AND OTHER
DISORDERS*

Art Unit: 1646
Examiner: Unassigned

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TRANSMITTAL LETTER

Commissioner for Patents
Arlington, VA 22202

Dear Sir:

Transmitted herewith is a Preliminary Amendment for filing in connection
with the above-identified application.

- ☒ The Commissioner is hereby authorized to charge any fee, including any
submitted herewith if the attached check(s) is in the wrong amount or otherwise
improper or missing, that may be due in connection with this and the attached
papers, or with this application during its entire pendency to or to credit any
overpayment to Deposit Account No. 50-1213. A duplicate of this sheet is
enclosed.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By:

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PRELIMINARY AMENDMENT

Commissioner for Patents
Arlington, VA 22202

Dear Sir:

Preliminary to examination of the above-captioned patent application, please amend the application as follows:

IN THE SPECIFICATION:

Please amend the specification as follows (a marked-up copy of the amended specification is attached to this Amendment):

Please replace the paragraph beginning on page 3, line 26, through page 4, line 8, with the following paragraph:

Cells known to produce IL-1ra include monocytes, neutrophils, macrophages and fibroblasts. Cytokines known to upregulate IL-1Ra production include IL-13, IL-6, IL-4, IFN- γ , GM-CSF and TGF- β , the latter apparently by triggering IL-1 production which itself triggers IL-1Ra synthesis. The amino acid sequences of IL-1Ra from at least four species have been determined (human, rat, mouse and rabbit) and found to be at least 75% homologous (Cominelli *et al.* (1994) *J. Biol. Chem.* 269:6963). IL-1Ra can also be synthesized as a strictly intracellular form whose production is the result of an alternative splicing of exon 1 (Butcher *et al.* (1994) *J. Immunol.* 153:701; Arend *et al.* (1993) *Adv. Immunol.* 54:167). IL-1Ra is released *in vivo* during experimentally-induced inflammation and as part of the natural course of many diseases. Administered experimentally, IL-1Ra has been demonstrated to block IL-1 activity *in vitro* and *in vivo*.

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